REMARKS

This Request for Continued Examination and Amendment is being submitted in response to the final Office Action dated November 5, 2009 in the above-identified application. If it is determined that any additional fee is due in connection with this filing, the Commissioner is authorized to charge said fees to Deposit Account No. 50-0552.

Claims 1-31 were originally pending. Applicants previously canceled the original claims and presented the elected claims as new claims 32-37 and added claims 38-46. Accordingly, claims 32-46 were pending for purposes of the instant action. All claims stand rejected.

Claim 32 has been amended. Support for the amendment to claim 32 can be found in the present specification, for example, in paragraphs [0039], [0070] and [0237] and Examples 3 to 6 of U.S. Publication No. 2006/0167092 of the present specification.

Claim 35 has been amended and now discloses a method for the treatment of cancer metastases. Claims 36-37 and 41-44 have been cancelled. Claims 38 and 46 have been amended so as to correct a typographical error. Claim 39 has been amended for clarity.

New claim 47 has been added for consideration. Claim 47 is dependent from claim 32 and discloses a method for the treatment of glioma. Support for new claim 47 can be found in examples 3 and 4 in the present application as filed (paragraphs [0193]-[0205]).

Applicants respectfully submit that no new matter has been added by the above amendments to the claims.

Claims 32 to 35, 38 to 40, 45 to 47 are now pending.

Reconsideration of these currently pending claims is respectfully requested.

Claim Objections

In the office action, the Examiner states that "claim 32 has been amended to introduce the phrase "as compared to the control level of metalloproteinase "MMP) or calpain found in a normal mammal" alleging that the aformentioned phrase does not have any literal support in the specification as filed.

To expedite the prosecution of the present application, claim 32 has been amended without prejudice to delete the phrase "as compared to the control level of metalloproteinase (MMP) or calpain found in a normal mammal".

In view of the foregoing, withdrawal of the objection to claim 32 is respectfully requested.

Claim Rejections under 35 U.S.C. § 112

Claims 32 to 46

In the Office Action, the Examiner maintained the rejection of claims 32 to 46 under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement and written description requirement. Specifically, the Examiner maintained his § 112 1st rejection to claims 32-46 allegedly "due to the lack in the scope of enablement requirement in inflammatory diseases, autoimmune diseases and cancer".

Independent claim 32 has been amended in relevant part to recite a method of treating MMPs or calpain related disease or disorder selected from cancer metastasis and glioma. Applicants respectfull submit that the present application shows for the first time, that lipophilic diesters of the general formula (I) (also called DP-BAPTAs) are useful for the inhibition of the proteolytic activities of MMPs. Examples 3 and 4 of the present invention (paragraphs [0193]-[0205]) specifically disclose the DP-BAPTA (e.g. DP-b99 and DP-b109) inhibitory activity on MMPs in human glioma cells (i.e. brain tumor). The present invention discloses that DP-BAPTAs not only inhibit MMPs activity, but further reduce MMP expression and release. In addition, it is to be emphasized that the critical role of MMPs and their inhibitors in human brain tumors

such as gliomas was known at the time of the invention (for example: Rooprai HK and McCormick D, "Proteases and their inhibitors in human brain tumors: a review, Anticancer Res., 1997, 17(6B):4151-62). Furthermore, it was well known in the art at the time the invention was made that MMP activity is a hallmark of cancer metastasis. The ability of MMPs to degrade the extracellular matrix proteins (such as collagens, elastins, laminins, fibronectins and the protein core of proteoglycans) leads to the proteolytic breakdown of tissue barriers to invasion and facilitate circulating tumor cell extravasation (for example see the following reviews: (i) Stamenkovic I, "Matrix metalloproteinases in tumor invasion and metastasis", seminars in cancer biol., 2000, 10:415-33 and (ii) Curran S. and Murray GI, "Matrix metalloproteinases in tumour invasion and metastasis", J. Pathol., 1999, 189(3):300-8). Support for "cancer metastasis" as recited in amended claim 32 can be found in paragraph [0070] of the present specification.

In view of the foregoing, withdrawal of the rejection of claims 32 to 46 under 35 U.S.C. §112, first paragraph is respectfully requested.

Claims 32 to 34, 38 to 40, 43, 45, and 46

In the Office Action, the Examiner rejected claims 32 to 34, 38 to 40, 43, 45, and 46 under §112 second paragraph. Specifically, the Office Action states that the phrase "a disease associated with an elevated metalloproteinase (MMP) or calpain in a mammal" is vague and indefinite because of its reach-through claim." See Office Action, page 4, third full paragraph. In the Office Action, the examiner "recommends to add the specific diseases to the claims." See Office Action, page 4, third full paragraph.

Claim 32 of the present invention has been amended in relevant part to encompass metalloproteinase (MMP) or calpain related disease or disorder selected from the group consisting of cancer metastasis and glioma.

In view of the foregoing, withdrawal of the rejection of claims 32 to 34, 38 to 40, 43, 45, and 46 under §112 second paragraph is respectfully requested.

Rejection of the Claims under 35 U.S.C. § 102(b) and 35 U.S.C. § 103(a)

In the Office Action, Claims 32 to 39 and 44-46 stand rejected under 35 U.S.C. § 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Kozak, et al. (WO 99/16741).

Independent claim 32 has been amended in relevant part to recite: "A method for treating or managing a metalloproteinase (MMP) or calpain related disease or disorder in a mammal, the disease or disorder being selected from the group consisting of cancer metastatis and glioma comprising administering to a mammal in need thereof, a pharmaceutical composition comprising a therapeutically effective amount of a compound of the Formula (I):..."

Kozak, et al. (WO 99/16741) discloses stable diesters of chelating agents of divalent metal ions, processes for their preparation and pharmaceutical compositions thereof, which are useful in a method for treating a condition or disease related to an excess of divalent metal ions, and in particular for the treatment of a condition or disease related to elevated levels of intracellular calcium ions. See abstract, Kozak, et al. (WO 99/16741).

35 U.S.C. § 102(b)

Applicants respectfully note that Examiner has not rejected claims 40 to 43 under 35 U.S.C. § 102 and therefore claims 40-43, which disclose in part methods for the treatment of cancer and cancer metastasis comprising the administration of lipophilic diesters of the general formula (I), are assumed to be novel and inventive in view of the prior art.

As described above, claim 32 of the present invention has been amended to encompass the administration of lipophilic diesters of the general formula (I) for the treatment of cancer metastasis and glioma, both are diseases which are claimed for the first time in the present application.

In view of the foregoing, WO 99/16741 did not teach or suggest "A method for treating or managing a metalloproteinase (MMP) or calpain related disease or disorder in a mammal, the disease or disorder being selected from the group consisting of cancer metastatis and glioma comprising administering to a mammal in need thereof, a pharmaceutical composition comprising a therapeutically effective amount of a compound of the Formula (I):..." as recited in independent claim 32 of the present invention.

Because the cited reference does not describe each and every element of the current claims, the cited reference cannot anticipate the claimed invention.

The present Response refers primarily to independent claim 32 of the present invention, however, the patentability of the dependent claims 33-39 and 44-46 follow at least for the reason of being dependent from the independent claim that is patentable.

Reconsideration and withdrawal of the rejection under 35 102(b) is respectfully requested.

35 U.S.C. § 103(a)

In the Office Action, the Examiner maintained the rejection of claims 32-39 and 44-46 under 35 U.S.C. § 103(a) as obvious over Kozak, et al. (WO 99/16741).

Applicants respectfully note that Examiner has not rejected claims 40 to 43 under 35 U.S.C. § 102 and therefore claims 40-43, which disclose in part methods for the treatment of cancer and cancer metastasis comprising the administration of lipophilic diesters of the general formula (I), are assumed to be novel and inventive in view of the prior art.

As described above, claim 32 of the present invention has been amended to encompass the administration of lipophilic diesters of the general formula (I) for the treatment of cancer metastasis and glioma, both are diseases which are claimed for the first time in the present application.

In view of the foregoing, WO 99/16741 did not teach or suggest "A method for treating or managing a metalloproteinase (MMP) or calpain related disease or disorder in a mammal, the disease or disorder being selected from the group consisting of cancer metastatis and glioma comprising administering to a mammal in need thereof, a pharmaceutical composition comprising a therapeutically effective amount of a compound of the Formula (I):..." as recited in independent claim 32 of the present invention.

In view of the foregoing, the claimed invention, as expressly recited, is unobvious in view of the Kozak disclosure.

This Response refers primarily to independent claim 32 of the present invention, however, the patentability of the dependent claims 33-39 and 44-46 follow at least for the reason of being dependent from independent claim that is patentable.

Reconsideration and withdrawal of the rejection of claims 32-39 and 44-46 under 35 USC 103(a) is respectfully requested.

CONCLUSION

A timely and favorable action in the subject application is respectfully urged.

Respectfully submitted,
DAVIDSON, DAVIDSON & KAPPEL, LLC

By: _____
Sunil Raval, Reg. No. 47,886

Davidson, Davidson & Kappel, LLC
485 Seventh Avenue, 14th floor
New York, NY 10018
(212) 736-1940